

CLAIMS:

1. A vascular damaging agent which is a compound of formula IA

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A-X-B

IA

Wherein

10

A is a substituted *cis*-stilbene moiety

X is a linker bond, atom or group

B is a moiety derived from an inhibitor of the formation or action of nitric oxide in mammalian systems said moiety having said inhibitor properties and attached to the molecule by a valency bond

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and the hydrates, pharmaceutically acceptable salts and prodrugs thereof.

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2. A vascular damaging agent which is a compound of formula I

A-X-B

I

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Wherein

A is a substituted *cis*-stilbene moiety

X is a linker bond, atom or group

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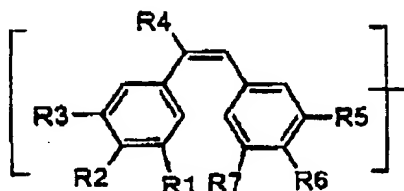
B is a moiety derived from an inhibitor of nitric oxide synthase said moiety having inhibitor properties and attached to the molecule by a valency bond

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and the hydrates, pharmaceutically acceptable salts and prodrugs thereof.

3. A vascular damaging agent according to claim 2 in which the *cis*-stilbene moiety is a group of formula II

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II

Wherein

- 10 R1, R2 and R3 are each independently H, optionally substituted alkoxy, optionally substituted alkyl or halogen
 R4 is hydrogen or cyano
 15 R5, R6 and R7 are each independently H, hydroxy, optionally substituted alkoxy, optionally substituted alkyl, halogen, amino, alkylamino, dialkylamino, cyano, nitro, carboxyl, alkanoyl, alkoxycarbonyl, alkoxycarbonyloxy, alkoxycarbonylamino, aminocarbonylamino, alkylaminocarbonylamino, dialkylaminocarbonylamino, alkylcarbonylamino, alkylsulphonyl, aminosulphonyl, alkylaminosulphonyl, dialkylaminosulphonyl, alkylsulphonylamino, aminosulphonylamino, alkylaminosulphonylamino, dialkylaminosulphonylamino, mercapto, alkylsulphanyl or
 20 alkylsulphinyl,

with the proviso that at least two of R1, R2 and R3 must be optionally substituted alkoxy.

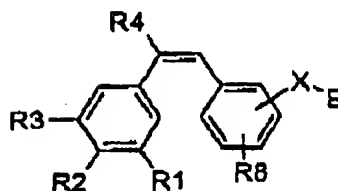
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4. An agent according to either of claims 2 and 3 in which the linker group X is a bond.

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5. An agent according to either of claims 2 and 3 in which the linker group is selected from an optionally substituted methylene chain, or $-(CH_2)_m-Y-(CH_2)_n-$ wherein Y is selected from $-O-$, $-S-$, $-S(O)-$, $-SO_2-$, $-NH-$, $-Nalkyl-$, $-CO-$, $-OC(O)-$, $-NHC(O)-$, $-N(alkyl)C(O)-$, $-NHC(O)NH-$, $-NalkylC(O)NH-$, $-NalkylC(O)Nalkyl-$, $-NHSO_2-$, $-NalkylSO_2-$, $-NHSO_2NH-$, $-NalkylSO_2NH-$, $-NalkylSO_2Nalkyl-$ and $-OC(O)O-$, m is 0-3 and n is 0-3.
6. An agent according to any one of claims 2 to 5 in which the nitric oxide synthase inhibitor moiety is selected from a group derived from an amino acid inhibitor of nitric oxide synthase, a thiocitrulline derivative, an S-alkylisothiourea derivative or 2-aminopyridine derivative.
7. An agent according to claim 6 in which the group derived from an amino acid inhibitor of nitric oxide synthase is a group $-C(O)CH(NH_2)-(CH_2)_p-NHC(NH)Z$ wherein p is 1-5 and Z is alkyl, alkylamino, dialkylamino, nitroamino, hydrazino or alkylthio, or a group $-NHCH(CO_2R_{10})-(CH_2)_p-NHC(NH)Z$ where p and Z are as hereinbefore described and R_{10} is hydrogen or alkyl.
8. An agent according to claim 6 in which the thiocitrulline group is $-C(O)CH(NH_2)-(CH_2)_p-NHC(S)NH_2$ or a group $-NHCH(CO_2R_{10})-(CH_2)_p-NHC(S)NH_2$.
9. An agent according to claim 6 in which the derivative of S-alkylisothiourea is $-(CH_2)_p-SC(NH)NH_2$.
10. An agent according to claim 6 in which the derivative of 2-aminopyridine is 4-methyl-2-pyridinylamino.
11. An agent according to claim 2 wherein the compound is

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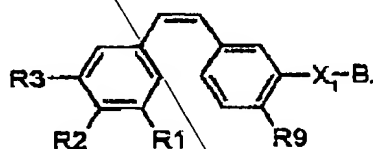
III

Wherein

- 5 R1, R2, R3, R4, X and B are as hereinbefore described
R8 is alkyl, amino, hydroxy, alkoxy or halogen

12. An agent according to claim 11 wherein the compounds are of formula III wherein R1, R2, R3, R4, are as hereinbefore described, R8 is alkyl, amino, hydroxy, alkoxy or halogen, X is -O- or -NH- and B is a group -C(O)CH(NH₂)-(CH₂)_p-NHC(NH)Z wherein p is 1-5 and Z is alkyl, alkylamino, dialkylamino, nitroamino, hydrazino or alkylthio or a group -NHCH(CO₂R₁₀)-(CH₂)_p-NHC(NH)Z where p, Z and R₁₀ are as hereinbefore described.

- 15 13. An agent according to claim 1 wherein the agent is of formula



IV

Wherein

- 20 R1, R2 and R3 are as hereinbefore described
R9 is alkyl, alkoxy or halogen
X₁ is O or NH
B₁ is a group -C(O)CH(NH₂)-(CH₂)_p-NHC(NH)Z wherein p is 1-5 and Z is alkyl, alkylamino, dialkylamino, nitroamino, hydrazino or alkylthio.

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14. An agent according to claim 2 which is selected from

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(Z)-1-(4-Methoxy-3-N^G-nitroarginyloxyphenyl)-2-(3,4,5-trimethoxyphenyl)ethene
 (Z)-N-[2-methoxy-5-[2-(3,4,5-trimethoxyphenyl)ethenyl]phenoxy carbonyl]N^G-
 nitroarginine methyl ester
 (Z)-N-[2-methoxy-5-[2-(3,4,5-trimethoxyphenyl)ethenyl]phenoxy carbonyl]N^G-
 nitroarginine
 (Z)-N-[2-methyl-5-[2-(3,4,5-trimethoxyphenyl)ethenyl]phenoxy carbonyl]N^G-
 nitroarginine methyl ester

7/6/21

15. Use of a substituted stilbene compound in preparation of a medicament for the treatment of diseases involving neovascularisation characterised in that the stilbene compound is of formula IA

A-X-B

IA

Wherein

A is a substituted *cis*-stilbene moiety

X is a linker bond, atom or group

B is a moiety derived from an inhibitor of the formation or action of nitric oxide in mammalian systems said moiety having inhibitor properties and attached to the molecule by a valency bond

and the hydrates, pharmaceutically acceptable salts and prodrugs thereof.

16. Use of a substituted stilbene compound in preparation of a medicament for the treatment of diseases involving neovascularisation characterised in that the stilbene compound is of formula I

A-X-B

I

5 Wherein

A is a substituted *cis*-stilbene moiety

X is a linker bond, atom or group

B is a moiety derived from an inhibitor of nitric oxide synthase said moiety having
10 inhibitor properties and attached to the molecule by a valency bond

and the hydrates, pharmaceutically acceptable salts and prodrugs thereof.

17. A method for the treatment of diseases involving neovascularisation
15 characterised by the administration of a stilbene derivative of formula I

A-X-B

IA

20

Wherein

A is a substituted *cis*-stilbene moiety

X is a linker bond, atom or group

25 B is a moiety derived from an inhibitor of the formation or action of nitric oxide in
mammalian systems said moiety having inhibitor properties and attached to the
molecule by a valency bond

and the hydrates, pharmaceutically acceptable salts and prodrugs thereof.

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18. A method for the treatment of diseases involving neovascularisation
characterised by the administration of a stilbene derivative of formula I

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